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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,547	10/17/2001	Jim Wells	SUNESIS.002DV1	8070

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/981,547	Applicant(s) WELLS ET AL.	
	Examiner Jon D Epperson	Art Unit 1639	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-80* is/are pending in the application.

4a) Of the above claim(s) *40-57,62-64 and 66-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-61 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Please note: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Status of the Application

1. Receipt is acknowledged of a Response to Restriction Requirement, which was dated on December 16, 2002 (Paper No. 8).

Priority Claims

2. The effective filing date of the claims is the filing date of the case i.e., October 17, 2001 (see New Matter Rejection below).

Status of the Claims

3. Claims 40-80 are pending in the present application in accordance with applicants transmittal sheet and Preliminary Amendments.

4. Applicant's response to the Restriction and/or Election of Species requirements in Paper No. 8 is acknowledged (Applicant elected Group IV, claims 58-66 with traverse) and claims 40-57 and 67-80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see below i.e., ***Response to Restriction and/or Election of Species***).

5. Claims 62-64 and 66 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in Paper No. 14 (see below i.e., ***Response to Restriction and/or Election of Species***).

6. Therefore, claims 58-61 and 65 are examined on the merits in this action.

Response to Restriction and Election of Species

7. Applicant's election of Group IV (claims 58-66) with traverse in Paper No. 8 is acknowledged.

8. The traversal is on the ground(s) that "Groups I and IV both concern methods for identifying ligands that bind to target protein. The claims within these two claims have similar scopes, and raise similar issues. Accordingly, examining these two groups in the same application does not place ... undue burden on the Examiner, rather would greatly facilitate the prosecution of the application" (see Paper No. 8, especially page 2).

9. These arguments were fully considered but were not found persuasive. Groups I and IV represent separate and patentably distinct methods. The methods are distinct because they use different steps, require different reagents and/or will produce different results. In this case, the method of Group I employs steps for "screening a library of small organic compounds" with a target protein-ligand conjugate, whereas Group IV only involves method steps for "identifying a

ligand" that binds to a target protein via mass spectrometry analysis. As a result, Group I requires different reagents and method steps (i.e., reagents and method steps for "screening a library of small organic compounds") that are not required by Group IV. Likewise, Group IV requires reagents and method steps (e.g., a mass spectrometer) that are not required by Group I. Consequently, Group I and Group IV can be separately classified e.g., Group I would be variously classified depending on the screening techniques used class 435/6, 7.1, DIG 18 and Group IV would be in areas for ligand binding and mass spectrometry such as class 436/501 and 250/281. In addition, since Groups I and IV do not utilize the same materials and method steps they will produce different results. Therefore, Groups I and IV have different issues regarding patentability and enablement and represent patentably distinct subject matter.

10. Furthermore, Groups II-IV represent separate and patentably distinct inventions because Group II is drawn to a product, Group III is drawn to an apparatus and Group IV is drawn to a method. The Groups are unrelated and are classified in separate classifications e.g., Group II is variously classified in class 530, subclass 402 and in other classes depending on the structure of the ligand e.g., classes 534 through 570; Group III is variously classified in class 250, subclass 281, 287, 288, 289 and Group IV can be classified in class 436, subclass 501 and class 250, subclass 282.

11. Therefore, the groups that describe these products and methods (i.e., Groups I-IV) have different issues regarding patentability and enablement, and represent patentably distinct subject matter, which merits separate and burdensome searches. Art anticipating or rendering obvious

each of the above-identified groups respectively would not necessarily anticipate or render obvious another group, because they are drawn to different inventions that have different distinguishing features and/or characteristics. Each group will support separate patents.

12. The current "Groups" are reiterated below to preserve the clarity of record (Applicants elected Group IV, claims 58-66 in Paper No. 8):

I. Claims 40-56, drawn to a process comprising "(a) screening a library of small organic compounds with a target protein-ligand conjugate ... and (b) identifying a small organic compound", classified variously in class 435, DIG 18; class 435, subclass 7.1.

II. Claims 57 and 77-80, drawn to a product described as a "synthetic organic ligand", classified in class 530, subclass 402 and in other class depending on the structure of said ligand e.g., classes 534 through 570.

III. Claims 67-76, drawn to an apparatus described as a "mass spectrometer", classified variously in class 250, subclass 288; class 250, subclass 282; class 250, subclass 283.

IV. Claims 58-66, drawn to a method for "identifying a ligand" using mass spectroscopy, classified variously in 436/501 and 250/281.

13. Applicant's election of species in Paper No. 8 with traverse is also acknowledged.

14. The election of species traversal is on the ground(s) that "it was impossible to elect a species of ligand along the lines suggested (for Group I) in the Office Action [Applicants were required to make the same elections for Group IV as indicated for Group I, see Paper No. 7, paragraph 6]. Cytokines, such as interleukins, are not listed as species of the ligand to be identified. In claim 45, the term "ligand" refers to the phrase ligand for a receptor" as it is used in claim 41, i.e., it further specifies a subgroup of the target proteins. Furthermore, since the ligand to be identified is a member of a small molecule library, which is identified only by its molecular weight and by the nature of the reactive group it carries, it is impossible to identify a single ligand molecule. Accordingly the Examiner is respectfully requested to reconsider and withdraw the requirement to elect a single species of the ligand for examination purposes" (see Paper No. 8, especially page 2).

15. These arguments were fully considered but were not found persuasive. The Examiner's position is that the species are distinct, each from the other, because the structures and modes of action of each of the species encompassed are different. Each of the ligands would have a different structure and would consequently be classified into various different classifications depending on that structure. Consequently, different species would require different searches and there is no expectation that the searches would be coextensive. Therefore, the Examiner maintains that this does create an undue search burden. However, solely in light of applicants ***admission*** that they are ***unable to select a single species*** (see Paper No. 8, page 2, paragraph 7, "[a]pplicants further note that it was impossible to elect a species of ligand") and in the interests

of furthering compact prosecution, applicants election of species is deemed acceptable (see Paper No. 8, especially page 2).

Furthermore, the Examiner previously stated that should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. This has not been done.

16. The current required species elections are reiterated below for Group IV to preserve the clarity of record (claim 58 is generic):

Subgroup 1: Species of target protein (see claim 58 and claims 62-66)

Applicant must elect, for the purposes of search, a ***single species*** of target protein e.g., mdm2 receptor.

Subgroup 2: Species of ligand (see claims 58-61)

Applicant must elect, for the purposes of search, a ***single species*** of ligand e.g., cytokine.

Subgroup 3: Species of chemically reactive group (see claims 40, 48-51)

Applicant must elect, for the purposes of search, a ***single species*** of chemically reactive group e.g., primary amine.

17. In order to allow applicant to make any additional arguments that were not possible to make in response to the incomplete Restriction Requirement of record (i.e., Paper No. 7), the Restriction Requirement has NOT been made FINAL.

Information Disclosure Statement

18. The information disclosure statement filed February 16, 2002, fails, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because two publications cited therein, numbered 16 and 20, lack publication dates, a necessary element for consideration. While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, these three publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPE § 609 C(1).

Specification

19. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 58-61 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (NEW MATTER). Claim(s) 58-61 and 65 were added in the Preliminary Amendment dated February 13, 2002 (Paper No.5). However, applicant did not specifically show where support for all these addition(s) could be found in the specification (please note Applicants statement that the "size limits of the ligands is at least at page 16, lines 24-31" do not specifically point to support for "all" the limitations in "all" the claims added e.g., where is the support for identifying the "inorganic" ligands that would be encompassed by claim 58). If applicant believes this rejection is in error, applicant must disclose where in the specification support for new claims 58-61 and 65 can be found. As a result, claims 58-61 and 65 represent new matter.

Please note that an amendment filed along with the filing of an application (as in the present Preliminary Amendment) does not enjoy the status as part of the original disclosure in an application filed under 37 CFR 1.53(b) unless it is specifically referred to in the oath or declaration filed therewith (e.g., see MPEP 608.04b). In the present instance, the oath or declaration fails to specifically refer to the Preliminary Amendment in its "reviewed and understands" clause (which is lacking); nor does the present declaration indicate that a CIP was intended to be filed by applicant.

22. Claims 58-61 and 65 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

These claims encompass a broad genus. For example, claim 58 outlines method steps for identifying a "ligand" that binds to a "site of interest" on a "target protein" wherein said ligand covalently binds to said target protein via a "chemically reactive group", wherein no structural features or identifying characteristics are provided for the "ligands" (Please note: the Examiner cannot find any support for the "inorganic" ligands that would be encompassed by claim 58, see New Matter Rejection above), "chemically reactive groups" or "target proteins" and no guidance is provided for determining where the "site of interest" might reside on said target proteins. The scope of this claim includes an infinite number of methods for identifying an "infinite" number of possible ligands that would bind to an "infinite" number of potential sites on an "infinite" number of proteins that have not been "specifically" disclosed by Applicants. Furthermore, the specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the "ligands" or the "chemically reactive groups" and likewise no structural or identifying features has been set forth for the "target proteins." In addition, the specification and claims do not provide ***any*** guidance as to where these "sites of interest" might reside on these undisclosed target proteins. Consequently, it is not possible to determine *a priori* which "ligands", "chemically reactive groups", "target proteins" and "sites of interest" would be encompassed by the present claims because there is no

commonality that can link together ***all*** of these unknown variables i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* what "ligands", "chemically reactive groups", "target proteins" and "sites of interest" should be included in this genus from the absence of working examples provided by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, ***not general***, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, simply reciting a "laundry list" of potential ligands, chemically reactive groups and target proteins (e.g., see specification, page 8, last paragraph, wherein target protein may be "enzymes, such as proteases and thymidylate synthease, steroid receptors, nuclear proteins, allosteric enzyme inhibitors, clotting factors ... etc.") is insufficient to teach the entire genus. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus. Thus, applicants were not in possession of the claimed genus.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 58-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Erlanson et al (Erlanson, D. A.; Braisted, A. C.; Raphael, D. R.; Randal, M.; Stroud, R. M.; Gordon, E. M.; Wells, J. A. *PNAS* **August 15, 2000**, *97(17)*, 9367-9372) (IDS Ref 15).

For ***claim 58***, Earlanson et al (see entire document) discloses [a] a method for identifying a ligand (see Erlanson et al, abstract), [b] less than 2000 daltons in size (see Erlanson et al, abstract), [c] that binds covalently to a chemically reactive group at a site of interest on a target protein (see Erlanson et al, abstract, see also figure 1 with schematic representation of a ligand binding covalently to a site of interest on a target protein via a "covalent" disulfide bond), [d] to for a target protein ligand conjugate (see Erlanson et al, figure 1 showing schematic of protein-ligand conjugate), and [e] comprising detecting the formation of said target protein-ligand conjugate by mass spectrometry analysis (see entire document, especially figure 2, see also page 9369, Results and Discussion Section).

For ***claims 59-61***, Erlanson et al discloses ligands that are ~ 250 daltons (see Erlanson et al, abstract).

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

26. Claims 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pitner et al (U.S. Pat. No. 5,367,058) (Date of Patent is November 22, 1994) and Ganem et al (Ganem, B.; Li, Y. T.; Henion, J. D. "Detection of noncovalent receptor-ligand complexes by mass spectrometry" *Journal of the American Chemical Society* **1991**, 113(16), 6294-6).

For **claims 58**, Pitner et al (see entire document) teaches [a] a method for identifying a ligand less than 2000 daltons in size (see Pitner et al, figures 6-7, see also column 4, paragraph 5, see also Examples 1-9, showing PC ligands that are ~250 Da), [b] that bind to a chemically reactive group (see Pitner et al, figure 1, showing chemically reactive group could be either SH or NH, see also column 3 lines 49-58), [c] at a site of interest on the target protein (see Pitner et al, figure 1, disclosing the "antigen binding site" as the "target of interest", see also column 3, paragraph 1), [d] to form a target

protein-ligand conjugate (see Pitner et al, figure 1, see also figures 6-7, see also Examples 1-9).

For **claims 59-61**, Pitner et al discloses PC ligands that are ~250 Da (see Pitner et al, entire document, especially figures 1, 6-7 and Examples 1-12).

The prior art teachings of Pitner et al differ from the claimed invention as follows:

For **claims 58**, Pitner et al is deficient in that it does not specifically teach the use of "mass spectrometry" for detecting the protein-ligand conjugate.

However, Ganem et al teaches the following limitations that Pitner et al lacks:

For **claim 58**, Ganem et al teaches the use of mass spectroscopy for "identifying enzyme-substrate, receptor-ligand ... complexes" (see Ganem et al, page 6294, paragraph 1; see also, page 6295, second column, last paragraph. Furthermore, Ganem et al teaches that the ligand can be "identified" using mass spectrometry (see Ganem et al, page 6296, "This result indicates that noncovalently bound species can be detected directly in a complex mixture without chromatographic separation").

It would have been obvious to one skilled in the art at the time the invention was made to "identify" a "ligand" that binds to a "target protein" wherein said "ligand" possesses a "chemically reactive group" and covalently binds to said "target protein" wherein said ligand is less than 2000 daltons as taught by Pitner et al in conjunction with the mass spectrometer techniques as taught by Ganem et al because Ganem et al explicitly states that the mass spectrometry "can be applied to problems of biological interest [including] ... proteins" and that the methods are good for "detecting and identifying enzyme-substrate, receptor-ligand [complexes]", (see Ganem et al, page 6294,

paragraph 1), which would encompass the "antibody-antigen" complexes of Pitner et al. Furthermore, one of ordinary skill in the art would have been motivated to use the mass spectrometers as taught by Ganem et al with the ligand-receptors as taught by the teachings of Pitner et al because Ganem et al explicitly states that the "ion-spray MS can be performed in water without cosolvent, which is ideal for most biological systems. Multiple charging produces a family of molecular ions and dramatically reduces the mass-to-charge ratio so that even quadrupole mass spectrometers having a typical range of 1000-2000 daltons (DA) can determine high MW species with unit mass resolution" (see Ganem et al, page 6294, second paragraph) (see also Ganem et al, page 6296, last paragraph).

27. Claims 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pitner et al (U.S. Pat. No. 5,367,058) (Date of Patent is November 22, 1994) and Loo, J. A. (Loo, J. A. "Studying Noncovalent Protein Complexes by Electrospray Ionization Mass Spectrometry" *Mass Spectrometry Reviews*, **1997**, *16*, 1-23).

For **claims 58**, Pitner et al (see entire document) teaches [a] a method for identifying a ligand less than 2000 daltons in size (see Pitner et al, figures 6-7, see also column 4, paragraph 5, see also Examples 1-9, showing PC ligands that are ~250 Da), [b] that bind to a chemically reactive group (see Pitner et al, figure 1, showing chemically reactive group could be either SH or NH, see also column 3 lines 49-58), [c] at a site of interest on the target protein (see Pitner et al, figure 1, disclosing the "antigen binding

site" as the "target of interest", see also column 3, paragraph 1), [d] to form a target protein-ligand conjugate (see Pitner et al, figure 1, see also figures 6-7, see also Examples 1-9).

For **claims 59-61**, Pitner et al discloses PC ligands that are ~250 Da (see Pitner et al, entire document, especially figures 1, 6-7 and Examples 1-12).

The prior art teachings of Pitner et al differ from the claimed invention as follows:

For **claims 58**, Pitner et al is deficient in that it does not specifically teach the use of "mass spectrometry" for detecting the protein-ligand conjugate.

However, Loo teaches the following limitations that Pitner et al lacks:

For **claim 58**, Loo teaches the use of mass spectroscopy for the "identification of novel protein-ligand interactions" including "antibody-antigen" conjugates (see Loo, entire document, especially page 14, section VI, paragraph 2, see also page 2, paragraph 1; see also abstract).

It would have been obvious to one skilled in the art at the time the invention was made to "identify" antibody/antigen interactions using the method steps as taught by Pitner et al in conjunction with the mass spectrometer techniques for the "identification of novel protein-ligand interactions" as taught by Loo because Loo explicitly states that the mass spectrometry can be applied to a broad range of protein-ligand interactions including "antibody-antigen" complexes (see Loo, page 2, paragraph 1), which would encompass the "antibody-antigen" complexes of Pitner et al. Furthermore, one of ordinary skill in the art would have been motivated to use the mass spectrometers as taught by Loo with the antibody-antigen conjugates as taught by Pitner et al because Loo

explicitly states that mass spectroscopy offers many advantages including speed, sensitivity, stoichiometry and mass accuracy (see Loo, abstract, see also page 4, column 1) for analyzing the protein/ligand interactions and their binding affinities.

Double Patenting

28. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

29. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

30. Claims 58-61 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,335,155 B1.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are drawn essentially to same method of identifying a ligand and, as a result, the inventions overlap in scope. For example, both references recite [a] methods for identifying a "ligand" (compare claim 1 of '155 to claim 58 of the present application), [b] wherein the ligand is < 500 Da (compare claim 1 of '155 to claims 58-61 of the present application, the present application is <2000 but the scope overlaps for <500), [c] wherein the target of interest is a protein (compare claim 4 of '155 to claim 58 of the present application), [d] using mass spectroscopic analysis (compare claim 1 (c) of '155 to claim 58 of the present application), [e] wherein the target protein is a TNF receptor (compare claim 1 of '199 to claim 65, note that in '199 applicant defines the "biological target molecule" as a TNF receptor i.e., see '199, specification column 5, paragraph 2 for definition of "biological target molecule"). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other.

31. Claims 58-61 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent Application Publication 2002/0081621 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are drawn essentially to same method of identifying a ligand and, as a result, the inventions overlap in scope. For example, both references recite [a] methods for identifying a "ligand" (compare claim 1 of '621 to claim 58 of the present application), [b] wherein the ligand is < 2000 Da ('621 does not add this limitation, but would encompass all ligand and thus ligand < 2000 Da i.e., the

claims would overlap in scope), [c] wherein the target of interest is a protein (compare claim 2, 18 and 33 of '621 to claim 58 of the present application), [d] using mass spectroscopic analysis (compare claims 11 and 31 of '621 to claim 58 of the present application), [e] wherein the target protein is a TNF receptor (compare claim 1 of '199 to claim 65, note that in '199 applicant defines the "biological target molecule" as a TNF receptor i.e., see '621, specification, paragraph bridging columns 2-3). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

32. Claims 58-61 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent Application Publication 2002/0155505 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are drawn essentially to same method of identifying a ligand and, as a result, the inventions overlap in scope. For example, both references recite [a] methods for identifying a "ligand" (compare claim 1 of '505 to claim 58 of the present application), [b] wherein the ligand is < 2000 Da ('505 does not add this limitation, but would encompass all ligands and thus ligands < 2000 Da i.e., the claims would overlap in scope), [c] wherein the target of interest is a protein (compare claim 7, 8, 16, 17, 23, of '505 to claim 58 of the present application), [d] using mass spectroscopic analysis (compare claims 1, 2, 10, 18, 21, 22 of '505 to claim 58 of the present application), [e] wherein the target protein is a TNF receptor (compare claims 1 of '199 to claim 65, note that in

'199 applicant defines the "preferred protein targets" as a TNF receptor i.e., see '505, specification, paragraph 87). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

33. Claims 58-61 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent Application Publication 2002/0022233 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are drawn essentially to same method of identifying a ligand and, as a result, the inventions overlap in scope. For example, both references recite [a] methods for identifying a "ligand" (compare claim 1 of '233 to claim 58 of the present application), [b] wherein the ligand is < 2000 Da ('233 does not add this limitation, but would encompass all ligands and thus ligands < 2000 Da i.e., the claims would overlap in scope), [c] wherein the target of interest is a protein (compare claim 2, 18 and 33 of '233 to claim 58 of the present application), [d] using mass spectroscopic analysis (compare claims 11 and 31 of '233 to claim 58 of the present application), [e] wherein the target protein is a TNF receptor (compare claims 1 of '199 to claim 65, note that in '199 applicant defines the "biological target molecule" as a TNF receptor i.e., see '233, specification, paragraph 30). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

34. Claims 58-61 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent Application Publication 2003/0013125 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are drawn essentially to same method of identifying a ligand and, as a result, the inventions overlap in scope. For example, both references recite [a] methods for identifying a "ligand" (compare claim 49 of '125 to claim 58 of the present application), [b] wherein the ligand is < 2000 Da ('125 does not add this limitation, but the compounds shown in claim 1 of '125 would be < 2000 Da i.e., the claims would overlap in scope), [c] wherein the target of interest is a protein ('125 does not add this limitation in the claims, but it does define the "target" in claim 49 as a protein i.e., see '125 specification, paragraph 130, see also figure 5 and this is to be compared with claim 58 of the present application), [d] using mass spectroscopic analysis ('125 does not add this limitation to the claims but does define the method of identification as mass spectroscopic analysis (see '125, specification, paragraphs 226-227 for definition and most preferred embodiments, see also figure 2, Example 8) and this is to be compared to claim 58 of the present application), [e] wherein the target protein is a TNF receptor (compare claims 1 of '199 to claim 65, note that in '199 applicant defines the "preferred protein targets" as a TNF receptor i.e., see '125, specification, paragraph 132). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Status of Claims/Conclusion

35. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

37. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

38. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
February 7, 2003